

Could 130/80 mmHg Be Adopted as the Diagnostic Threshold and Management Goal of Hypertension in Consideration of the Characteristics of Asian Populations?

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This commentary discusses the practical feasibility of the 2017 American Heart Association/American College of Cardiology (AHA/ACC) guidelines¹ for the management of hypertension and the ideal direction of blood pressure (BP) prevention, detection, evaluation, and management for achieving a goal of zero cardiovascular events in Asia.

Hypertension is a massive global burden on healthcare that indiscriminately affects both high- and low-income countries. However, there are significant ethnic differences in the determinants of hypertension and cardiovascular disease.^{2,3} The 2017 AHA/ACC guidelines for the prevention, detection, evaluation, and management of high BP in adults changed the diagnostic threshold and the management goal of BP from 140/90 to 130/80 mmHg. This change in the BP threshold raises 2 important practical considerations for the treatment of hypertension in Asian countries. Because of the stronger BP-dependent characteristics of cardiovascular disease in Asians compared with Westerners, the reduction to a BP goal of 130/80 mmHg is right in the front of the figure universal management of hypertension. However, because of various cultural and socioeconomic factors specific to Asian countries, the BP control in these countries was not sufficient even when the 140/90 mmHg threshold was used. The shift of the BP threshold to 130/80 mmHg level will significantly increase the number of patients with hypertension or uncontrolled hypertension to ≈50% of all Asian adults living in Asian countries.

The opinions expressed in this editorial are not necessarily those of the editors or of the American Heart Association.

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Benefit of Earlier Treatment Initiation Based on the 130/80 mmHg BP Threshold

The goal of the management of hypertension is not reducing BP per se but rather preventing cardiovascular events. From this view point, earlier diagnosis and treatment of hypertension is effective for reducing cardiovascular events later in life. The diagnosis of hypertension is based on the average of BP measurements taken, but cardiovascular events may be triggered by BP surge (a pressor component of BP variability).

There are various phenotypes of BP variability with different time phases. In order from shortest to longest, these include beat-by-beat, acute trigger-specific (with triggers, such as physical and mental stress, strain, cold temperature, and poor sleep), positional, diurnal, day-by-day, seasonal, and yearly BP variability. When the peaks of these pressor components of BP variability (BP surges) are synchronized, a dynamic surge BP is generated (ie, the resonance hypothesis of BP surge; Figure 1).^{4,5} In younger individuals, each BP surge is small, and the synchronized BP surge is physiological. With aging, however, the amplitude of each BP surge increases, and the synchronized dynamic BP surge becomes pathological, with greater potential to trigger cardiovascular events. Especially in high-risk patients with cardiovascular risk factors, the exaggerated dynamic BP surge can reach peripheral sites without absorption at the stiffened aorta, resulting in the triggering of cardiovascular events.

The age-related increase in the dynamic BP surge would be much steeper than that in the average BPs. Thus, considering that the average BP-based diagnosis and goal seems to underestimate the risk of dynamic BP surge, the earlier treatment of hypertension based on an average BP diagnostic threshold and management goal of 130/80 mmHg will do much more to reduce the cumulative risk burden of exaggerated surge BP than the previous threshold of 140/90 mmHg (Figure 1). Moreover, the benefit may be greater in the Asian population than in Westerners when we consider the following characteristics of Asian populations.

Asian Characteristics of Hypertension

We recently presented a consensus report on improving the hypertension management in Asian patients by taking into account the various characteristics unique to this population.⁶ For example, the phenotypes of cardiovascular disease, stroke, and heart failure, which are closely associated with BP, are more common in Asia. Moreover, the association between

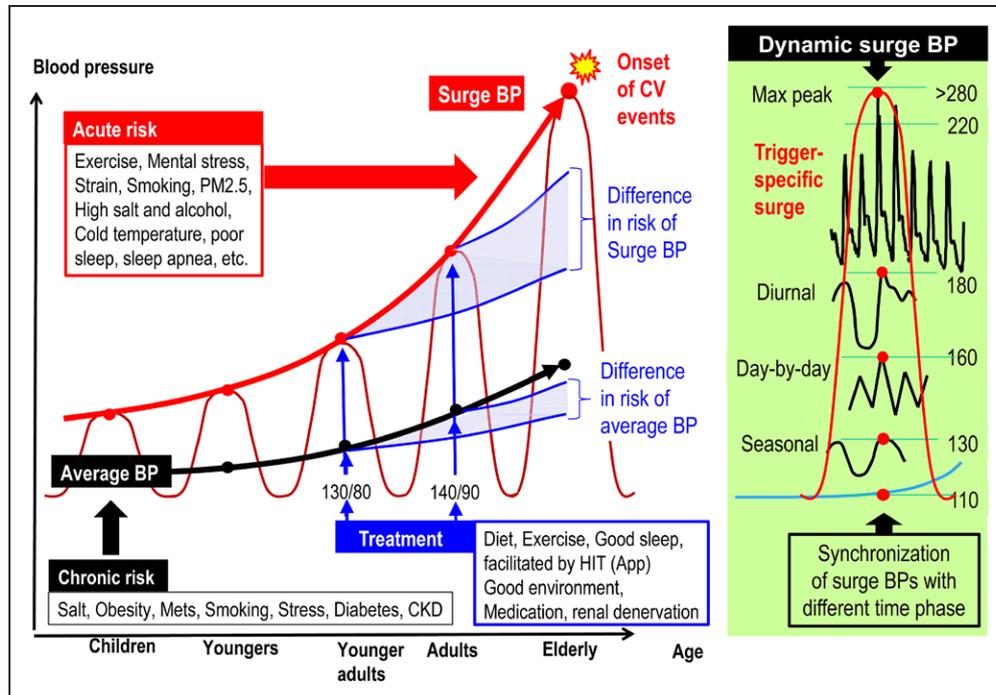


Figure 1. The impact of age-related risk reduction of surge blood pressure (BP) by the shift of the average BP from 140/90 to 130/80 mmHg as the diagnostic threshold and treatment goal of hypertension. The earlier intervention has a greater protective effect on the age-related cardiovascular burden of exaggerated (dynamic) surge BP. The dynamic surge BP is generated by the synchronization of surge BPs with different time phases (this is known as the Resonance hypothesis). App indicates application software; CKD, chronic kidney disease; CV, cardiovascular; HIT, health information technology (such as applications for remote monitoring and self-monitoring of BP); and PM2.5, particulate matter 2.5.

hypertension and cardiovascular disease is stronger in Asian countries than Western countries. In addition, stroke is more common than coronary artery disease in Asian people, whereas the reverse is true in Western populations. In the recent prospective HONEST study (Home Blood Pressure Measurement With Olmesartan Naive Patient, to Establish Standard Target BP), the incidence of stroke was 2.8× higher than that of myocardial infarction (2.92 versus 1.03/1000 person-years) in on-treatment hypertensive patients.⁷ The slope of the association between higher BP levels and cardiovascular events has also been shown to be steeper in Asians compared with Western populations.⁸ In consideration of these Asian-specific characteristics, antihypertensive medication targeting a lower systolic BP (SBP; eg, <130 mmHg) would be of greater benefit in Asians than in Westerners, especially for reducing the risk of stroke and heart failure.

A country-based, regional approach factoring in ethnic differences in the pathogenesis and clinical characteristics of hypertension is important for effective practical management. In our previous survey of the consciousness of the management of hypertension in Asia, 87% of all Asian physicians answered that they did take into consideration the Asian lifestyle and Asian-specific characteristics of hypertension, and 92% recognized the need for Asian-specific guidelines for the management of hypertension.⁹ Furthermore, the acquisition of global comparative evidence for the efficacy of different drugs could contribute to the development of region-specific guidelines for hypertension management. Although this approach is also relevant and applicable to Europe, it can be argued that the call to action is greater and more urgent in

Asia. This is because, given the wider disparities in practice and in healthcare delivery and infrastructure in these rapidly developing countries, any efforts aimed at formally standardizing and optimizing key management practices could have a more immediate impact on treatment gaps. Moreover, there is less available evidence in Asian populations, and thus further clinical studies to clarify Asian-specific characteristics would ultimately improve the management of hypertension.

HOPE Asia Network

We recently established the HOPE Asia Network (Hypertension, Brain, Cardiovascular and Renal Outcome Prevention and Evidence in Asia).¹⁰ The HOPE Asia Network is made up of several groups of Asian hypertension researchers—for example, the Asia BP@Home Investigators' Meeting and the COME Asia-MHDG (Characteristics on the Management of Hypertension in the Asia-Morning Hypertension Discussion Group)—which have been studying and discussing the characteristics of hypertension and cardiovascular–renal disease in Asian populations. Its ultimate mission is to improve the management of hypertension and organ protection toward the achievement of zero cardiovascular events in Asia. The activity of the HOPE Asia Network is based on 3 initiatives: (1) examining and analyzing all of the existing evidence-related to hypertension, (2) forming a consensus on hot clinical topics of hypertension, and (3) conducting Asia-wide clinical studies of hypertension. In addition, the HOPE Asia Network is proud to be a member organization of The World Hypertension League and looks forward to contributing actively to World Hypertension League's mission of confronting the global

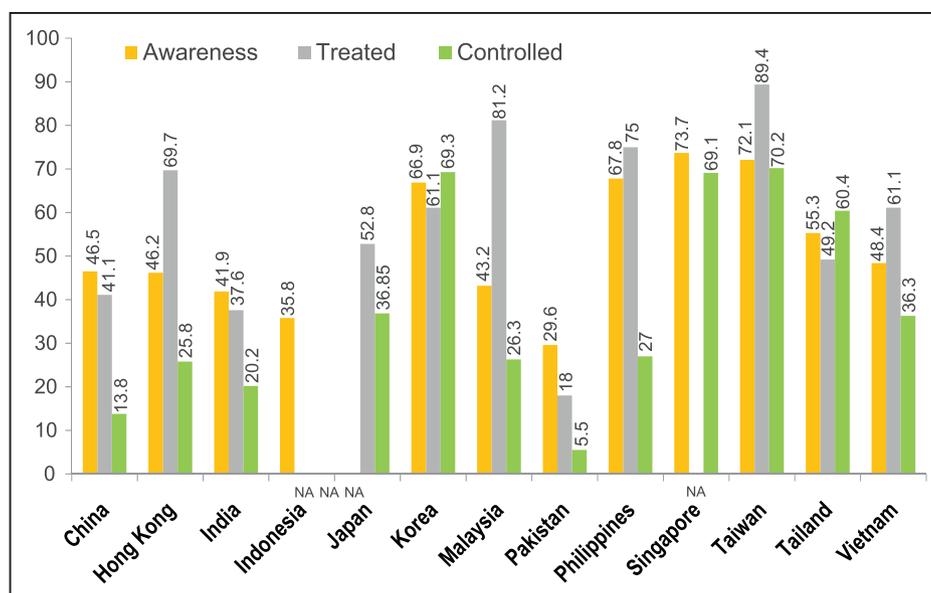


Figure 2. Awareness, treatment, and control rate of hypertension in Asian countries and regions. NA indicates data not available.

epidemic of hypertension and the huge burden of premature death and disability that results from this condition.

As a first step in pursuing the objectives of the HOPE Asia Network, we have collected studies in the literature concerning the status of BP control in Asian countries (Figure 2).^{11,12} This body of evidence suggests that the awareness, treatment, and control rates of hypertension are generally low in Asia but also markedly different among the individual Asian countries. Even within single Asian countries, the broad regional, economic, and cultural differences seem to affect BP and BP control. The hypertension data in Figure 2 were defined by the 140/90 mm Hg threshold. As the new threshold from the 2017 AHA/ACC guidelines, 130/80 mm Hg is increasingly adopted, the BP control rate of hypertension is expected to decrease dramatically. Already in the United States, application of the new criteria has resulted in an increase in the prevalence of hypertension and uncontrolled BP, especially in younger adults.¹³ This increase should be even more pronounced in Asian countries than in Western countries. One of the effects of this change may be an increase in the cost of anti-hypertensive medication worldwide. However, the increased prevalence of hypertension does not necessarily mean that a strict medication regimen should be recommended. Instead, lifestyle modifications started earlier in life (diet, exercise, good sleep, good environment, etc) facilitated by health information technology (eg, applications for smart phone or computer), especially reducing salt intake and body weight, are recommended as a first-line treatment in Asia (Figure 2).

Obesity and Salt Intake in Asia

The impact of obesity on high BP may differ between Asians and whites. Asians are likely to develop high BP even with mild obesity. From the viewpoint of the risk of the 2017 AHA/ACC Elevated BP/Stage I hypertension (previous prehypertension), the impact of body mass index 25 kg/m² in Japanese is almost equivalent to that of body mass index 30 kg/m² in the US population.¹⁴ Obesity and metabolic syndrome are

known to increase salt sensitivity. Asians are likely to have a genetic predisposition to salt sensitivity.¹⁵ Compounding this problem, Asians tend to have a higher salt intake.¹⁶ Thus, the increase in salt sensitivity caused even by mild obesity could readily cause high BP in Asians who are already prone to high salt sensitivity and high salt intake.

Salt intake is gradually decreasing in Japan but remains high at >10 g/d. In our survey in hypertensive patients recruited from general practitioner-based clinics in Tochigi prefecture, the average salt intake (estimated by concentrations of sodium and creatinine in spot urine) was 10.2 g/d, and the prevalence of well-controlled patients with a salt intake of <6 g/d was only 6.7%.¹⁷ We confirmed that a moderate salt restriction of -1.8 g/d (targeted 6.0 g/d, baseline 8.6 g/d, achieved 6.8 g/d), directed by a nutritionist, will significantly reduce clinic, home, and ambulatory BP (-7.3 mm Hg for 24-hour SBP) in medicated hypertensive patients.¹⁸

Thus, salt restriction to salt intake <6.0 g/d and body weight moderation to body mass index <25 kg/m² are effective approaches, especially in Asians.

Twenty-Four-Hour Ambulatory BP Profile in Asia

The 2017 ACC/AHA guidelines recommend that hypertension be managed using home BP monitoring and ambulatory BP monitoring.¹ A 24-hour BP profile is determined partly by an individual's genetic factors, but it is also strongly affected by a variety of cultural factors (eg, food, lifestyle, and traditions) and environmental factors (eg, temperature, atmospheric pressure, humidity, and seasonal changes).^{4,5}

BP variability may be greater in the Asian than the Western population.⁶ Exaggerated morning surge in BP may be more prevalent in Asian people, and, even when clinic BPs are normal, Asians are more likely to have morning and nocturnal hypertension. It is, therefore, important to assess out-of-clinic BP in Asian patients, especially first in the morning, and ideally during the sleep period as well. A recent analysis of data

from the international ambulatory BP monitoring registry, the ARTEMIS study (International Ambulatory Blood Pressure Registry: Telemonitoring of Hypertension and Cardiovascular Risk Project), demonstrated that the prevalence of masked hypertension is higher in Asians than in Westerners.¹⁹ In the same database, even though the clinic BP is comparable between Japanese and Western hypertensive patients, the Japanese hypertensive patients have an exaggerated morning surge in BP compared with their Western counterparts.²⁰ In the patients with drug-resistant hypertension, who were recruited according to the same global entry criteria of the Simplicity HTN-3 and HTN-Japan trials for catheter-based renal denervation, even when the clinic BP was comparable, Japanese patients had higher morning BP level and greater morning BP surge than the white and black patients.²¹

In addition, Asians are likely to have isolated nocturnal hypertension.²² In population cohorts, the nocturnal BP fall may be less in Asians than in the Westerners.²³ In addition, isolated nocturnal hypertension is significantly associated with arterial stiffness in the Chinese population.²⁴ Nocturnal hypertension is associated with high sodium intake and salt sensitivity,²⁵ which seems to be specific characteristics of hypertension in Asian populations. The international epidemiological data have demonstrated that increased nocturnal BP is a powerful predictor of cardiovascular outcomes, especially in treated hypertensive patients.²⁶ Thus, the impact of controlling hypertension for a 24-hour period would be greater in Asians.⁶

Facilitation of a Home BP-Guided Approach in Asia

As a second step in the activities of the HOPE Asia Network, we have focused on home BP values. Specifically, we have focused on a morning home BP-guided approach as the most effective strategy to achieve zero cardiovascular events in Asia.^{27–30}

The Japanese Society of Hypertension Guidelines for the Management of Hypertension (JSH 2014) first documented a home BP-guided approach as the most effective practical approach in clinical practice.³¹ The 2017 ACC/AHA guidelines recommended home BP monitoring for confirmation of

the diagnosis of hypertension and for titration of BP-lowering medication, in conjunction with telehealth counseling (recommendation: Class I; Level of Evidence A). Early detection and control of masked hypertension are the keys for successful individual management of 24-hour BP control.² An information communication technology-based anticipation approach using individual time-series big BP data is expected to dramatically suppress the incidence of cardiovascular events and improve the health and longevity of patients worldwide.^{4,5}

Four Asian studies have demonstrated that morning home BP is a better prognostic predictor of cardiovascular events than clinic BP. These were the general population-based Ohasama Study,³² the general practitioner-based J-HOP study (Japan Morning Surge-Home Blood Pressure),³³ a hypertensive outpatient trial on medication (HOMED-BP, Hypertension Objective Treatment Based on Measurement by Electrical Devices of Blood Pressure),³⁴ and the largest nationwide Japanese real-world observational study (HONEST).^{7,35} Indeed, in the HONEST study, a morning home SBP of ≈ 125 mmHg was associated with minimal risk for both stroke and coronary artery disease events.

Because of Asian lifestyle, individuals are unlikely to measure their evening home BP before dinner, and thus it is recommended that the evening home BP be measured just before going to bed.^{27–30} We stressed the importance of morning home BP in clinical practice^{27–30} because morning home BP has shown better reproducibility than evening home BP or clinic BP.³⁶ However, the measurement of evening home BP just before going to bed is strongly affected by the individual's dinner (including alcohol consumption) and evening behavior (eg, bathing in the evening is common in Asia).³⁷ Thus, morning home BP control is important from a practical standpoint, especially in Asian hypertensive patients.

The next step after controlling morning home BP is the management of uncontrolled nocturnal hypertension. The 2017 AHA/ACC guidelines defined a threshold of nocturnal BP (110/65 mmHg) corresponding to clinic, home, and daytime BPs (all 130/80 mmHg).¹ Figure 3 shows the nighttime and morning home SBP control status in the J-HOP study. A morning home SBP of 135 mmHg corresponds to

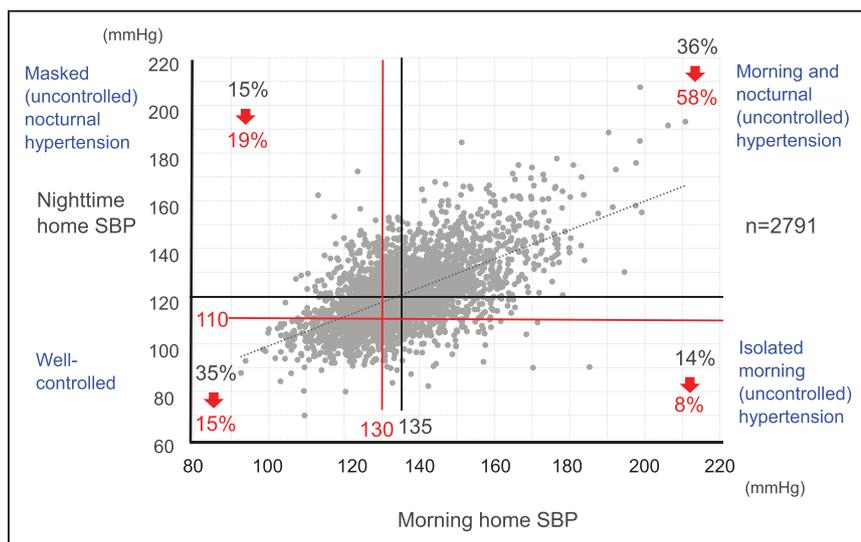


Figure 3. Shift in the prevalence of nocturnal hypertension classified by the new American Heart Association/American College of Cardiology 2017 guidelines (red) from that classified by the previous Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure guidelines (black) in subjects in the J-HOP study (Japan Morning Surge-Home Blood Pressure; 2791 medicated hypertensives). SBP indicates systolic blood pressure.

a night-time home SBP of 120 mmHg, which is the threshold defined by the Seventh Report of the Joint National Committee on Prevention while the 110 mmHg threshold of the 2017 ACC/AHA guidelines corresponds to a morning home SBP of 130 mmHg. In those with well-controlled morning home SBP, a significant proportion of patients continue to have uncontrolled nocturnal hypertension (30% by the criteria of 135 mmHg for morning home SBP and 120 mmHg for night-time SBP; 56% by the criteria of 130 mmHg for morning home SBP and 110 mmHg for night-time SBP). Thus, even after controlling morning BP, there is still a remaining risk of uncontrolled nocturnal hypertension. The new criteria for night-time BP threshold from the 2017 ACC/AHA guidelines might not contribute to a reduction in masked uncontrolled hypertension. Thus, to detect the residual risk of uncontrolled nocturnal hypertension, ambulatory BP monitoring or nocturnal home BP monitoring would be recommended even in patients with well-controlled normotension for clinic BP and morning home BPs, especially in the high-risk Asian hypertensive patients having diabetes mellitus, chronic kidney disease, sleep apnea, or sustained organ damages, such as left ventricular hypertrophy or albuminuria.

As a feasibility study of the HOPE Asia Network, we have started the Asia BP@Home study, which will determine the prevalence of masked uncontrolled morning home BP and the characteristics of home BP variability in medicated hypertensive patients living in 12 Asian countries.³⁸ The Asia BP@Home study is the first cross-sectional study of home BP in Asia using the same protocol and the same home BP monitoring device in currently medicated hypertensive outpatients of participating countries. It seeks to identify the regional, country-based, and ethnic differences in the current BP control status. Through this and other HOPE Asia Network activities, we hope to contribute to advances in the management of hypertension and the prevention of cardiovascular–renal disease, with the ultimate goal of achieving zero cardiovascular events in Asia.

Conclusions and Perspectives

Regardless of whether we use the term hypertension to describe a BP status >130/80 mmHg, the core concept in the 2017 ACC/AHA guidelines—namely, earlier and tighter BP control over 24 hours—will contribute to more sustained target organ protection and cardiovascular disease prevention in Asia. To determine the feasibility and benefit of 130/80 mmHg as a diagnostic threshold and management goal of BP, we have begun to collect the previous Asian evidence to reach a consensus, and we are also promoting further clinical research in Asian countries by facilitating the HOPE Asia Network activity.

Disclosures

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Could 130/80 mm Hg Be Adopted as the Diagnostic Threshold and Management Goal of Hypertension in Consideration of the Characteristics of Asian Populations?

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